

THAT WHICH IS CLAIMED:

1. A composition comprising IFN- $\beta$  or variant thereof and highly purified mannitol.

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2. The composition of claim 1, wherein said composition is characterized by increased stability.

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3. The composition of claim 1, wherein said composition is lyophilized.

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4. The composition of claim 1, wherein said composition is a liquid.

5. The composition of claim 1, wherein said highly purified mannitol is present at a concentration of about 0.25% to about 5% by weight per volume.

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6. The composition of claim 1, wherein said IFN- $\beta$  or variant thereof is present at a concentration of 0.01 mg/ml to 15 mg/ml.

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7. The composition of claim 1, wherein said formulation has a pH within a range of about pH 3.0 to about pH 9.0.

8. The composition of claim 1, also comprising human albumin.

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9. The composition of claim 8, wherein said human albumin is present at a concentration of about 0.01% to about 15% by weight per volume.

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10. A composition comprising IFN- $\beta$  and highly purified mannitol, wherein said IFN- $\beta$  is recombinant human IFN- $\beta$ , said recombinant human IFN- $\beta$  is present at a concentration of about 0.01 mg/ml to about 15 mg/ml, said highly purified mannitol is present at a concentration of about 0.25 % to about 5% by weight per volume, the pH of

the composition is about 3.0 to about 9.0, and the composition additionally comprises human albumin at a concentration of about 0.01 % to about 15% by weight per volume.

11. The composition of claim 10, wherein said composition is lyophilized.

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12. The composition of claim 10, wherein said composition is a liquid or is frozen.

13. A composition comprising IFN- $\beta$  and highly purified mannitol, wherein  
10 said IFN- $\beta$  is recombinant human IFN- $\beta$ , said recombinant human IFN- $\beta$  is present at a concentration of about 0.01 mg/ml to about 15 mg/ml, said highly purified mannitol is present at a concentration of about 0.25 % to about 5% by weight per volume, the pH of the composition is about 3.0 to about 9.0, and the composition additionally comprises human albumin at a concentration of about 0.01 % to about 15% by weight per volume  
15 and sufficient sodium chloride to render the composition isotonic.

14. The composition of claim 13, wherein said composition is lyophilized.

15. The composition of claim 13, wherein said composition is a liquid or  
20 frozen.

16. A composition comprising IFN- $\beta$  and highly purified mannitol, wherein  
the IFN- $\beta$  is recombinant human IFN- $\beta$ , said recombinant human IFN- $\beta$  is present at a concentration of about 0.05 mg/ml to about 1 mg/ml, said highly purified mannitol is  
25 present at a concentration of about 0.25% to about 2.5% by weight per volume, the pH of the composition is about 6.8 to about 8.2, and the composition additionally comprises human albumin at a concentration of about 0.25% to about 2.5% by weight per volume.

17. The composition of claim 16, further comprising sufficient sodium  
30 chloride to render the composition isotonic.

18. The composition of claim 16, wherein said composition is a liquid, wherein said liquid is frozen or lyophilized.

5 19. The composition of claim 17, wherein said composition is a liquid, wherein said liquid is frozen or lyophilized.

10 20. A composition comprising IFN- $\beta$  and highly purified mannitol, wherein the IFN- $\beta$  is recombinant human IFN- $\beta$ , said recombinant human IFN- $\beta$  is present at a concentration of about 0.25 mg/ml, said highly purified mannitol is present at a concentration of about 1.25% by weight per volume, the pH of the composition is about 7.3 to about 7.5, and the composition additionally comprises human albumin at a concentration of about 1.25% by weight per volume.

15 21. The composition of claim 20, further comprising sufficient sodium chloride to render the composition isotonic.

20 22. The composition of claim 20, wherein said composition is a liquid, wherein said liquid is frozen or lyophilized.

23. The composition of claim 21, wherein said composition is a liquid, wherein said liquid is frozen or lyophilized.

25 24. The composition of claim 1, wherein said IFN- $\beta$  is the polypeptide with the amino acid sequence of mature native human IFN- $\beta$ .

25. The composition of claim 24, wherein said IFN- $\beta$  is glycosylated or unglycosylated.

26. The composition of claim 1, wherein said IFN- $\beta$  is recombinantly produced.

5 27. A pre-filled syringe comprising the composition of claim 1.

28. The pre-filled syringe of claim 27, wherein said composition is frozen.

10 29. A composition comprising IFN- $\beta$  or variant thereof and mannitol, wherein said mannitol has a reducing activity of less than 20 parts per million.

15 30. A composition comprising a pharmaceutical polypeptide and highly-purified mannitol.

20 31. The composition of claim 30, wherein said pharmaceutical polypeptide is selected from the group consisting of human growth hormone, interferon, interleukin, granulocyte-macrophage colony stimulating factor, granulocyte colony stimulating factor, macrophage colony stimulating factor, beta-glucocerebrosidase, thyrotropins, etanercept, monoclonal antibodies, factor VIIa, factor VIII, urokinase, asparaginase, anistreplase, and alteplase.

25 32. A method of producing a formulation of IFN- $\beta$  or a biologically active variant thereof characterized by improved stability, said method comprising producing a formulation comprising IFN- $\beta$  or biologically active variant thereof and highly purified mannitol in an amount sufficient to stabilize said IFN- $\beta$  or variant thereof.

33. A formulation made according to the method of claim 32.

34. A method of producing a formulation of IFN- $\beta$  or a biologically active variant thereof, comprising the steps of:

- a) removing sodium dodecyl sulfate and salts from the IFN- $\beta$  by chromatography;
- b) combining said IFN- $\beta$  with a solution of human albumin at a pH of about 11.5 to about 12.0;
- 5 c) adjusting the pH of the solution to 7.5 with HCl; and
- d) adding a solution of highly purified mannitol.

35. A formulation produced according to the method of claim 34.

10 36. The method of claim 34, further comprising the step of lyophilizing the formulation.

15 37. A method for increasing the stability of IFN- $\beta$  or variant thereof in a pharmaceutical composition, said method comprising incorporating into said composition highly purified mannitol in an amount sufficient to stabilize said IFN- $\beta$  or variant thereof.

38. The method of claim 34, further comprising the step of adding sufficient sodium chloride to render the composition isotonic.

20 39. A formulation produced according to the method of claim 38.

40. The method of claim 38, further comprising the step of lyophilizing the formulation.

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